



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,625	11/02/2006	Stephen J. Klaus	FP0617 US	7369
41385	7590	09/24/2009		
FIBROGEN, INC. 409 Illinois Street San Francisco, CA 94158			EXAMINER OGUNBIYI, OLUWATOSIN A	
			ART UNIT 1645	PAPER NUMBER
			MAIL DATE 09/24/2009	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/566,625	Applicant(s) KLAUS ET AL.	
	Examiner OLUWATOSIN OGUNBIYI	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 July 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,9-38 and 46-49 is/are pending in the application.
- 4a) Of the above claim(s) 17,18,34,35,37,38,46 and 47 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 9-16, 19-33, 36 and 48-49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/10/09 has been entered.

Claims 1,9-38 and 46-49 are pending in the application.

Claims 17,18, 34,35,37,38,46 and 47 are withdrawn.

Claims 1, 9-16, 19-33, 36 and 48-49 are under examination.

Rejections Withdrawn

1. The rejection of claims 1-5, 9, 10, 11-15, 19-21, 23-27 under 35 U.S.C. 101 as claiming the same invention as that of claim 1-9, 10, 11-15, 17-24, 34-56, of copending Application No.11/348294 ('294) is withdrawn in view of the amendment to the claims.

2. The rejection of claims 1-5, 9-16, 19, 21-25 and 48-49 under 35 U.S.C. 102(e) as being anticipated by Klaus et al. US 2003/0153503 published Aug 14, 2003, filed Dec. 6, 2002 as evidenced by Pace et al. Experimental Hematology 2000, 28:283-293 is withdrawn in view of the amendment to the claims.

3. The rejection of claims 1-5, 9-16, 19, 20, 21-25 and 48-49 under 35 U.S.C. 103(a) as being unpatentable over Klaus et al. US 2003/0153503 published Aug 14, 2003, filed Dec. 6, 2002 and Pace et al. Experimental Hematology 2000, 28:283-293 and Tung et al. WO 97/12855 April 10, 1997 is withdrawn in view of the amendment to the claims.

Art Unit: 1645

4. The rejection of claims 1-5, 9-16, 19, 21-33, 36 and 48-49 is rejected under 35 U.S.C. 103(a) as being unpatentable over Klaus et al. US 2003/0153503 published Aug 14, 2003, filed Dec. 6, 2002 and Pace et al. Experimental Hematology 2000, 28:283-293 and Bohmer et al WO 01/12784 A1 22 February 2001 is withdrawn in view of the amendment to the claims.

Rejections Maintained

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

5. The rejection of claim 16 provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 16 of copending Application No. 11/348,294 is maintained for the reasons below:

Both claim 16 of the instant application and claim 16 of the '294 application are drawn to a method for increasing the proportion of fetal hemoglobin relative to non- fetal hemoglobin produced by a cell or population of cells, the method comprising administering to the cell or population of cells an agent which increases expression of the gene encoding gamma-globin.

Art Unit: 1645

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

New Rejections Based on Amendment

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1, 9-16, 19 and 21-27 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9, 10, 11-16, 17-24, 34-56 of copending Application No.11/348294 ('294).

Claim 1 and dependent claims are drawn to a method for increasing endogenous gamma globin (gamma-globin) in a subject, the method comprising administering to the subject hypoxia inducible factor (HIF) prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma –globin in a cell selected from hematopoietic stem cells and BFU-E cells.

Art Unit: 1645

Claim 1 of the '294 application is drawn to method for increasing endogenous gamma globin (γ -globin) in a subject in need thereof, the method comprising administering to the subject hypoxia- inducible factor (HIF) prolyl hydroxylase inhibitor which increases expression of the gene encoding γ -globin. Said HIF prolyl hydroxylase inhibitor increases expression of the gamma-globin gene by inhibiting 2-oxoglutarate dioxygenase enzyme activity wherein the enzyme is EGLN1, EGLN2, EGLN3 (compare instant claim 9 to claims 6-9 of the '294 claims).

Claim 10 of the instant application is drawn to a method for increasing the level of fetal hemoglobin , the method comprising administering to the subject HIF prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma-globin. Claim 10 of the '294 application is drawn to a method for increasing the level of fetal hemoglobin in a subject in need thereof, the method comprising administering to the subject a HIF prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma -globin.

Claim 11 and dependent claims of the instant application is drawn to a method for treating a disorder associated with abnormal hemoglobin in a subject in need thereof, the method comprising administering to the subject a HIF prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma globin in a cell selected from hematopoietic stem cells and BFU-E cells, thereby increasing the level of fetal hemoglobin in the subject. Claim 11 and dependent claims of the '294 application is drawn to a method for treating a disorder associated with abnormal hemoglobin in a subject in need thereof, the method comprising administering to the subject a HIF prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma globin, thereby increasing the level of fetal hemoglobin in the subject

Art Unit: 1645

Claim 42 of the '294 application is drawn to a method for increasing the level of fetal hemoglobin in a subject in need thereof, the method comprising administering to the subject an a HIF prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma-globin, wherein the HIF prolyl hydroxylase inhibitor increases expression of the gene encoding gamma-globin by increasing the stability or activity of an alpha subunit of hypoxia inducible factor (HIF alpha). Claim 10 of the instant application is drawn to a method for increasing the level of fetal hemoglobin , the method comprising administering to the subject HIF prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma-globin in a cell selected from hematopoietic stem cells and BFU-E cells . Said HIF prolyl hydroxylase inhibitor inherently increases the stability or activity of an alpha subunit of hypoxia inducible factor (HIF alpha).

Claim 43 of the '294 application is drawn to a method for treating a disorder associated with hemoglobinopathy in a subject in need thereof, the method comprising administering to the subject an a HIF prolyl hydroxylase inhibitor which increases the level of fetal hemoglobin in the subject, wherein the HIF prolyl hydroxylase inhibitor increases the level of fetal hemoglobin in the subject by increasing the stability or activity of an alpha subunit of hypoxia inducible factor (HIF alpha). Claim 11 of the instant application is drawn to a method for treating a disorder associated with abnormal hemoglobin (a hemoglobinopathy) in a subject in need thereof, the method comprising administering to the subject a HIF prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma globin in a cell selected from hematopoietic stem cells and BFU-E cells , thereby increasing the level of fetal hemoglobin in the subject. Said

Art Unit: 1645

HIF prolyl hydroxylase inhibitor inherently increases the stability or activity of an alpha subunit of hypoxia inducible factor (HIF alpha).

Claim 48 of the '294 application is drawn to a method for increasing the proportion of fetal hemoglobin relative to non- fetal hemoglobin produced by a cell or population of cells, the method comprising administering to the cell or population of cells an agent which increases expression of the gene encoding gamma-globin, wherein the agent increases expression of the gene encoding gamma-globin by increasing the stability or activity of an alpha subunit of hypoxia inducible factor (HIF alpha). Claim 16 of the instant application is also drawn to a method for increasing the proportion of fetal hemoglobin relative to non- fetal hemoglobin produced by a cell or population of cells, the method comprising administering to the cell or population of cells an agent which increases expression of the gene encoding gamma-globin. Said agent inherently increases expression of the gene encoding gamma-globin by increasing the stability or activity of an alpha subunit of hypoxia inducible factor (HIF alpha).

The claims of the '294 application and the instant claims are drawn to similar inventions as set forth supra except that the '294 application does not state recite “ which increases expression of the gene encoding y-globin in a cell selected from hematopoietic stem cells and BFU-E cells”. However, it is inherent that the gamma globin gene expression occurs in hematopoietic stem cells and BFU-E cells, see claim 22-24 of the '294 application. The art teaches that expression of the gene encoding gamma globin inherently and normally occurs in erythroid progenitor cells such as BFU-E cells as evidenced by Perrine et al, see title and abstract, p. 454 under materials and methods, p. 457 column 2 second to last paragraph (cited in IDS) and or hematopoietic/erythroid bone marrow stem cells which retain the capability to

Art Unit: 1645

produce fetal hemoglobin which comprises gamma globin (see Ley et al p. 488 under "regulation and modulation of HBF synthesis in red blood cell precursors").

Claims 1, 9-16, 19 and 21-27 are directed to an invention not patentably distinct from claims 1-9, 10, 11-16, 17-24, 34-56 of commonly assigned copending Application No.11/348294 ('294) as set in the rejections above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned Application No.11/348294, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

7. Claims 1, 9-16, 19, 21-27, 28-33 and 36 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9, 10, 11-

Art Unit: 1645

16, 17-24, 34-56 of copending Application No.11/348294 ('294) in view of Bohmer et al WO 01/12784 A1 22 February 2001.

Claim 1 and dependent claims are drawn to a method for increasing endogenous gamma globin (gamma-globin) in a subject, the method comprising administering to the subject hypoxia inducible factor (HIF) prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma -globin in a cell selected from hematopoietic stem cells and BFU-E cells.

Claim 1 of the '294 application is drawn to method for increasing endogenous gamma globin (y-globin) in a subject in need thereof, the method comprising administering to the subject hypoxia- inducible factor (HIF) prolyl hydroxylase inhibitor which increases expression of the gene encoding y-globin. Said HIF prolyl hydroxylase inhibitor increases expression of the gamma-globin gene by inhibiting 2-oxoglutarate dioxygenase enzyme activity wherein the enzyme is EGLN1, EGLN2, EGLN3 (compare instant claim 9 to claims 6-9 of the '294 claims).

Claim 10 of the instant application is drawn to a method for increasing the level of fetal hemoglobin , the method comprising administering to the subject HIF prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma-globin. Claim 10 of the '294 application is drawn to a method for increasing the level of fetal hemoglobin in a subject in need thereof, the method comprising administering to the subject a HIF prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma -globin.

Claim 11 and dependent claims of the instant application is drawn to a method for treating a disorder associated with abnormal hemoglobin in a subject in need thereof, the method comprising administering to the subject a HIF prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma globin in a cell selected from hematopoietic stem cells

Art Unit: 1645

and BFU-E cells, thereby increasing the level of fetal hemoglobin in the subject. Claim 11 and dependent claims of the '294 application is drawn to a method for treating a disorder associated with abnormal hemoglobin in a subject in need thereof, the method comprising administering to the subject a HIF prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma globin, thereby increasing the level of fetal hemoglobin in the subject

Claim 42 of the '294 application is drawn to a method for increasing the level of fetal hemoglobin in a subject in need thereof, the method comprising administering to the subject an a HIF prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma-globin, wherein the HIF prolyl hydroxylase inhibitor increases expression of the gene encoding gamma-globin by increasing the stability or activity of an alpha subunit of hypoxia inducible factor (HIF alpha). Claim 10 of the instant application is drawn to a method for increasing the level of fetal hemoglobin , the method comprising administering to the subject HIF prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma-globin in a cell selected from hematopoietic stem cells and BFU-E cells . Said HIF prolyl hydroxylase inhibitor inherently increases the stability or activity of an alpha subunit of hypoxia inducible factor (HIF alpha).

Claim 43 of the '294 application is drawn to a method for treating a disorder associated with hemoglobinopathy in a subject in need thereof, the method comprising administering to the subject an a HIF prolyl hydroxylase inhibitor which increases the level of fetal hemoglobin in the subject, wherein the HIF prolyl hydroxylase inhibitor increases the level of fetal hemoglobin in the subject by increasing the stability or activity of an alpha subunit of hypoxia inducible factor (HIF alpha). Claim 11 of the instant application is drawn to a method for treating a disorder

Art Unit: 1645

associated with abnormal hemoglobin (a hemoglobinopathy) in a subject in need thereof, the method comprising administering to the subject a HIF prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma globin in a cell selected from hematopoietic stem cells and BFU-E cells, thereby increasing the level of fetal hemoglobin in the subject. Said HIF prolyl hydroxylase inhibitor inherently increases the stability or activity of an alpha subunit of hypoxia inducible factor (HIF alpha).

Claim 48 of the '294 application is drawn to a method for increasing the proportion of fetal hemoglobin relative to non- fetal hemoglobin produced by a cell or population of cells, the method comprising administering to the cell or population of cells an agent which increases expression of the gene encoding gamma-globin, wherein the agent increases expression of the gene encoding gamma-globin by increasing the stability or activity of an alpha subunit of hypoxia inducible factor (HIF alpha). Claim 16 of the instant application is drawn to a method for increasing the proportion of fetal hemoglobin relative to non- fetal hemoglobin produced by a cell or population of cells, the method comprising administering to the cell or population of cells an agent which increases expression of the gene encoding gamma-globin. Said agent inherently increases expression of the gene encoding gamma-globin by increasing the stability or activity of an alpha subunit of hypoxia inducible factor (HIF alpha).

The claims of the '294 application and the instant claims are drawn to similar inventions as set forth supra except that the '294 application does not state recite “ which increases expression of the gene encoding y-globin in a cell selected from hematopoietic stem cells and BFU-E cells”. However, it is inherent that the gamma globin gene expression occurs in hematopoietic stem cells and BFU-E cells, see claim 22-24 of the '294 application. The art

Art Unit: 1645

teaches that expression of the gene encoding gamma globin inherently and normally occurs in erythroid progenitor cells such as BFU-E cells as evidenced by Perrine et al, see title and abstract, p. 454 under materials and methods, p. 457 column 2 second to last paragraph (cited in IDS) and or hematopoietic/erythroid bone marrow stem cells which retain the capability to produce fetal hemoglobin which comprises gamma globin (see Ley et al p. 488 under "regulation and modulation of HBF synthesis in red blood cell precursors").

The '294 claims do not teach administering the HIF prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma globin to a population of cells and transfusing the gamma globin expressing cells into the subject.

Bohmer et al teaches a method for increasing the level of fetal hemoglobin in a subject having abnormal hemoglobin such as beta thalassemia and sickle cell syndrome such as sickle cell trait and sickle cell anemia comprising administering to a population of cells (such as hematopoietic stem cells) an agent which increase the number of fetal hemoglobin producing cells (resulting from increased expression of the gene encoding gamma globin) and transferring said cells into the subject (p. 2 lines 10-25, p. 17 claim 1, 5).

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to modify the method of the '294 claims so as to administer *ex vivo* to a population of cells that synthesize fetal hemoglobin such as hematopoietic cells said HIF prolyl hydroxylase inhibitor thus increasing gamma globin gene expression in said cells and transfusing said cells into said subjects (subjects with abnormal hemoglobin) of 'the 294 claims because Bohmer et al teaches that the level of fetal hemoglobin in hematopoietic cells of patients with abnormal hemoglobin can be increased *ex vivo* and said cells can be transfused back to said

Art Unit: 1645

subject in order to treat said abnormal hemoglobin conditions. Furthermore, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made that other erythroid progenitor cells such as BFU-E that have the capability of expressing gamma globin and synthesizing fetal hemoglobin can be treated *ex vivo* with said HIF prolyl hydroxylase inhibitor and a said cells transfused back to subjects in order to treat abnormal hemoglobin conditions.

This is a provisional obviousness-type double patenting rejection.

Claims 1, 9-16, 19, 21-27, 28-33 and 36 are directed to an invention not patentably distinct from claims 1-9, 10, 11-16, 17-24, 34-56 of commonly assigned copending Application No.11/348294 ('294) as set in the rejections above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned Application No.11/348294, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly

Art Unit: 1645

assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 28-33 and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for increasing the level of fetal hemoglobin levels in a subject, the method comprising administering to the a population of hematopoietic stem cells, BFU-E cells or bone marrow derived cells, a hypoxia inducible factor (HIF) prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma –globin and transfusing the gamma globin expressing cells into the subject, does not reasonably provide enablement for said method comprising administering to a population of other types of cells a hypoxia inducible factor (HIF) prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma –globin and transfusing the gamma globin expressing cells into the subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to a method for increasing the level of fetal hemoglobin levels in a subject, the method comprising administering to the a population of cells a hypoxia inducible

Art Unit: 1645

factor (HIF) prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma –globin and transfusing the gamma globin expressing cells into the subject.

The specification teaches increased gamma globin expression and induction of fetal hemoglobin in erythroid cell line that K562 using a hypoxia inducible factor (HIF) prolyl hydroxylase inhibitor (example 4 from p. 24) and induction of fetal hemoglobin in bone marrow cell cultures. The specification contemplates increasing endogenous gamma globin in hematopoietic stem cells, BFU-E cells and bone marrow cells p. 5 paragraph 16.

The scope of the claims encompasses administering a hypoxia inducible factor (HIF) prolyl hydroxylase inhibitor to any type of cell population which includes any type of organism derived cell including skin cells, brain cells, T cells, B cells bone marrow cells, BFU-E cells, hematopoietic stem cells etc.

The art teaches that expression of the gene encoding gamma globin normally occurs in erythroid progenitor cells such as BFU-E cells as evidenced by Perrine et al, see title and abstract, p. 454 under materials and methods, p. 457 column 2 second to last paragraph (cited in IDS) and or hematopoietic/erythroid bone marrow stem cells which retain the capability to produce fetal hemoglobin which comprises gamma globin (see Ley et al p. 488 under “regulation and modulation of HBF synthesis in red blood cell precursors”. Thus, only erythroid progenitor cells such as BFU-E cells, hematopoietic stem cells and bone marrow derived cells have the inherent capability of gamma globin gene expression and thus fetal hemoglobin expression.

The art at the time of the instant invention does not teach that other organism derived cells that are not erythroid progenitor cells have this capability of gamma globin gene expression and thus fetal hemoglobin production. The specification also does not provide any evidence for

Art Unit: 1645

such and does not specifically teach gamma globin gene expression in other types of cells such as brain cells or skin cells or T cells or B cells, to name a few.

Therefore, it is predicted that these other types of organism derived cells are not capable of gamma globin gene expression, thus administering said a hypoxia inducible factor (HIF) prolyl hydroxylase inhibitor to any of the other types of organism derived cells listed above will mostly likely not lead to increased gamma gene expression and an increase in the level of fetal hemoglobin in a subject as claimed.

Therefore, undue experimentation would be required of the skilled artisan to practice the instant invention as broadly claimed with a population of cells types that are not capable of gamma globin gene expression.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 25-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25 is drawn to increasing endogenous gamma in a cell i.e. any type of cell, whereas the same claims teaches that the expression of the gene coding gamma-globin is increased in either of two types of specific cells i.e. hematopoietic stem cells or blast-forming erythroid (BFU-E) cells. The recitation of the broader limitation of increasing endogenous gamma globin (gamma-globin) in any type of cell followed by the recitation of a narrower

Art Unit: 1645

limitation that the that the expression of the gene coding gamma-globin is increased in either of two types of specific cells i.e. hematopoietic stem cells or blast-forming erythroid (BFU-E) cells renders the claim indefinite. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 1, 9-16, 19, 21-27 and 48-49 are rejected under 35 U.S.C. 102(e) as being anticipated by Klaus et al. US 2003/0153503 published Aug 14, 2003, filed Dec. 6, 2002 as evidenced by Pace et al. Experimental Hematology 2000, 28:283-293, cited previously and as evidenced by Perrine et al (Blood, W.B. Saunders, Philadelphia, PA. U.S., 7/1/89, col. 74, No.1, p.454-459, cited in IDS) and as evidenced by Ley et al (Annu Rev Med, 1985, Vol. 36, pp.485-498, cited in IDS).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C.

Art Unit: 1645

102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention “by another,” or by an appropriate showing under 37 CFR 1.131.

The claims are drawn to a method for increasing endogenous gamma globin (gamma-globin) or increasing fetal hemoglobin levels in a subject, the method comprising administering to the subject hypoxia inducible factor (HIF) prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma –globin in a cell selected from the group consisting of hematopoietic stem cells and blast-forming erythroid (BFU-E) cells.

Klaus teaches a method for increasing endogenous erythropoietin *in vitro* and *in vivo* comprising administering a compound that inhibits HIF prolyl hydroxylase enzyme activity (p. 2 paragraph 19) which increases endogenous erythropoietin (see abstract, see p. 3 paragraph 14). Erythropoietin increases the expression of the gene encoding gamma globin thus increasing the level of fetal hemoglobin as evidenced by Pace et al. Experimental Hematology 2000, 28:283-293 (see first sentence of abstract and first paragraph of the introduction). Thus, said method of increasing endogenous erythropoietin of Klaus et al will increase endogenous gamma globin and thus increase fetal hemoglobin absent evidence to the contrary. It is known in the art that expression of the gene encoding gamma globin inherently and normally occurs in erythroid progenitor cells such as BFU-E cells as evidenced by Perrine et al, see title and abstract, p. 454 under materials and methods, p. 457 column 2 second to last paragraph (cited in IDS) and or hematopoietic/erythroid bone marrow stem cells which retain the capability to produce fetal hemoglobin which comprises gamma globin (see Ley et al p. 488 under “regulation and

Art Unit: 1645

modulation of HBF synthesis in red blood cell precursors". Thus, as to claims 25-27, the method of Klaus et al which administers said HIF prolyl hydroxylase inhibitor to a human (p. 1 paragraph 10) inherently increases the endogenous gamma globin in the cells such as hematopoietic stem cells or BFU-E cells of said human.

Further, Klaus et al teaches a method for increasing endogenous erythropoietin thus increasing expression of the gamma globin gene by administering an agent which inhibits 2-oxoglutarate dioxygenase enzyme activity such as enzyme activity of EGLN1, EGLN2, EGLN3 or any subunit or fragment thereof or inhibits HIF hydroxylase enzyme activity of HIF hydroxylase enzymes such as EGLN1, EGLN2, EGLN3 (p.2 paragraph 13).

Klaus et al teaches said method (which inherently increases fetal hemoglobin as set forth supra) to treat disorders associated with abnormal hemoglobin such as thalassemia major and minor (beta thalassemia), sickle cell disease (sickle cell syndrome, sickle cell anemia) (p. 11 paragraph 80). Said method would result in the increased proportion of fetal hemoglobin producing cells to non-fetal hemoglobin producing cells as erythropoietin acts at the cellular level by increasing gamma gene expression, thus increasing fetal hemoglobin. As set forth above, gamma globin gene expression inherently occurs in BFU-E Cells and hematopoietic/erythroid bone marrow stem cells.

Said agent of Klaus et al is administered with a second therapeutic agent such as exogenous erythropoietin or G-CSF (p.23 paragraph 187, p. 31 claim 15). The method of Klaus et al is performed *in vivo* or *ex vivo* (in vitro) (abstract) and the agent is administered to primates e.g. humans or a cell (p. 1 paragraph 10).

Art Unit: 1645

Klaus et al teaches that the compound is an hydroxamate (iron chelator – p. 31 claim 36) or structural mimetics of 2 oxo-glutarate (paragraph 110 p. 14). Said 2 oxoglutarate mimetic will inherently inhibit (HIF) prolyl hydroxylase competitively with respect to 2 oxoglutarate and non-competitively with respect to iron.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

Art Unit: 1645

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1, 9-16, 19, 21-27, 28-33, 36 and 48-49 are rejected under 35 U.S.C. 103(a) as being obvious over Klaus et al. US 2003/0153503 published Aug 14, 2003, filed Dec. 6, 2002 as evidenced by Pace et al. Experimental Hematology 2000, 28:283-293, cited previously and as evidenced by Perrine et al. Blood, W.B. Saunders, Philadelphia, PA. U.S., 7/1/89, col. 74, No.1, p.454-459, cited in IDS and as evidenced by Ley et al. Annu Rev Med, 1985, Vol. 36, pp.485-498, cited in IDS) in view of Bohmer et al WO 01/12784 A1 22 February 2001, cited previously.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the

Art Unit: 1645

reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The claims are drawn to a method for increasing the level of fetal hemoglobin levels in a subject, the method comprising administering to the a population of cells a hypoxia inducible factor (HIF) prolyl hydroxylase inhibitor which increases expression of the gene encoding gamma –globin and transfusing the gamma globin expressing cells into the subject.

Klaus teaches a method for increasing endogenous erythropoietin *in vitro* and *in vivo* comprising administering a compound that inhibits HIF prolyl hydroxylase enzyme activity (p. 2 paragraph 19) which increases endogenous erythropoietin (see abstract, see p. 3 paragraph 14). Erythropoietin increases the expression of the gene encoding gamma globin thus increasing the level of fetal hemoglobin as evidenced by Pace et al. Experimental Hematology 2000, 28:283-293 (see first sentence of abstract and first paragraph of the introduction). Thus, said method of increasing endogenous erythropoietin of Klaus et al will increase endogenous gamma globin and thus increase fetal hemoglobin absent evidence to the contrary. It is known in the art that expression of the gene encoding gamma globin inherently and normally occurs in erythroid progenitor cells such as BFU-E cells as evidenced by Perrine et al, see title and abstract, p. 454 under materials and methods, p. 457 column 2 second to last paragraph (cited in IDS) and or hematopoietic/erythroid bone marrow stem cells which retain the capability to produce fetal hemoglobin which comprises gamma globin (see Ley et al p. 488 under “regulation and modulation of HBF synthesis in red blood cell precursors”. Thus, as to claims 25-27, the method of Klaus et al which administers said HIF prolyl hydroxylase inhibitor to a human (p. 1

Art Unit: 1645

paragraph 10) inherently increases the endogenous gamma globin in the cells such as hematopoietic stem cells or BFU-E cells of said human.

Further, Klaus et al teaches a method for increasing endogenous erythropoietin thus increasing expression of the gamma globin gene by administering an agent which inhibits 2-oxoglutarate dioxygenase enzyme activity such as enzyme activity of EGLN1, EGLN2, EGLN3 or any subunit or fragment thereof or inhibits HIF hydroxylase enzyme activity of HIF hydroxylase enzymes such as EGLN1, EGLN2, EGLN3 (p.2 paragraph 13).

Klaus et al teaches said method (which inherently increases fetal hemoglobin as set forth supra) to treat disorders associated with abnormal hemoglobin such as thalassemia major and minor (beta thalassemia), sickle cell disease (sickle cell syndrome, sickle cell anemia) (p. 11 paragraph 80). Said method would result in the increased proportion of fetal hemoglobin producing cells to non-fetal hemoglobin producing cells as erythropoietin acts at the cellular level by increasing gamma gene expression, thus increasing fetal hemoglobin. As set forth above, gamma globin gene expression inherently occurs in BFU-E Cells and hematopoietic/erythroid bone marrow stem cells.

Said agent of Klaus et al is administered with a second therapeutic agent such as exogenous erythropoietin or G-CSF (p.23 paragraph 187, p. 31 claim 15). The method of Klaus et al is performed *in vivo* or *ex vivo* (in vitro) (abstract) and the agent is administered to primates e.g. humans or a cell (p. 1 paragraph 10).

Klaus et al teaches that the compound is an hydroxamate (iron chelator – p. 31 claim 36) or structural mimetics of 2 oxo-glutarate (paragraph 110 p. 14). Said 2 oxoglutarate mimetic will

Art Unit: 1645

inherently inhibit (HIF) prolyl hydroxylase competitively with respect to 2 oxoglutarate and non-competitively with respect to iron.

While Klaus et al teaches administering *ex vivo* the HIF prolyl hydroxylase inhibitor that increases endogenous gamma globulin thus fetal hemoglobin in cells such as hematopoietic stem cells and BFU-E cells as set forth supra, Klaus et al also does not teach administering the HIF prolyl hydroxylase inhibitor to a population of cells and transfusing the gamma globin expressing cells into the subject.

Bohmer et al teaches a method for increasing the level of fetal hemoglobin in a subject having abnormal hemoglobin such as beta thalassemia and sickle cell syndrome such as sickle cell trait and sickle cell anemia comprising administering to a population of cells (such as hematopoietic stem cells) an agent which increase the number of fetal hemoglobin producing cells (resulting from increased expression of the gene encoding gamma globin) and transferring said cells into the subject (p. 2 lines 10-25, p. 17 claim 1, 5).

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to modify the method of Klaus et al so as to administer *ex vivo* to a population of cells that synthesize fetal hemoglobin such as hematopoietic cells said HIF prolyl hydroxylase inhibitor of Klaus et al, thus increasing gamma globin gene expression in said cells and transfuse said cells into said subjects (subjects with abnormal hemoglobin) of Klaus et al because Bohmer et al teaches that the level of fetal hemoglobin in hematopoietic cells of patients with abnormal hemoglobin can be increased *ex vivo* and said cells can be transfused back to said subject in order to treat said abnormal hemoglobin conditions. Furthermore, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made

Art Unit: 1645

that other the erythroid progenitor cells such as BFU-E that have the capability of expressing gamma globin and synthesizing fetal hemoglobin can be treated *ex vivo* with said HIF prolyl hydroxylase inhibitor and said cells transfused back to subjects in order to treat abnormal hemoglobin conditions.

12. Claims 1, 9-16, 19, 20, 21-27 and 48-49 are rejected under 35 U.S.C. 103(a) as being obvious over Klaus et al. US 2003/0153503 published Aug 14, 2003, filed Dec. 6, 2002 as evidenced by Pace et al. Experimental Hematology 2000, 28:283-293, cited previously and as evidenced by Perrine et al. Blood, W.B. Saunders, Philadelphia, PA. U.S., 7/1/89, col. 74, No.1, p.454-459, cited in IDS and as evidenced by Ley et al. Annu Rev Med, 1985, Vol. 36, pp.485-498, cited in IDS in view of Tung et al. WO 97/12855 April 10, 1997, cited previously.

Klaus teaches a method for increasing endogenous erythropoietin *in vitro* and *in vivo* comprising administering a compound that inhibits HIF prolyl hydroxylase enzyme activity (p. 2 paragraph 19) which increases endogenous erythropoietin (see abstract, see p. 3 paragraph 14). Erythropoietin increases the expression of the gene encoding gamma globin thus increasing the level of fetal hemoglobin as evidenced by Pace et al. Experimental Hematology 2000, 28:283-293 (see first sentence of abstract and first paragraph of the introduction). Thus, said method of increasing endogenous erythropoietin of Klaus et al will increase endogenous gamma globin and thus increase fetal hemoglobin absent evidence to the contrary. It is known in the art that expression of the gene encoding gamma globin inherently and normally occurs in erythroid progenitor cells such as BFU-E cells as evidenced by Perrine et al, see title and abstract, p. 454 under materials and methods, p. 457 column 2 second to last paragraph (cited in IDS) and or

Art Unit: 1645

hematopoietic/erythroid bone marrow stem cells which retain the capability to produce fetal hemoglobin which comprises gamma globin (see Ley et al p. 488 under "regulation and modulation of HBF synthesis in red blood cell precursors". Thus, as to claims 25-27, the method of Klaus et al which administers said HIF prolyl hydroxylase inhibitor to a human (p. 1 paragraph 10) inherently increases the endogenous gamma globin in the cells such as hematopoietic stem cells or BFU-E cells of said human.

Further, Klaus et al teaches a method for increasing endogenous erythropoietin thus increasing expression of the gamma globin gene by administering an agent which inhibits 2-oxoglutarate dioxygenase enzyme activity such as enzyme activity of EGLN1, EGLN2, EGLN3 or any subunit or fragment thereof or inhibits HIF hydroxylase enzyme activity of HIF hydroxylase enzymes such as EGLN1, EGLN2, EGLN3 (p.2 paragraph 13).

Klaus et al teaches said method (which inherently increases fetal hemoglobin as set forth supra) to treat disorders associated with abnormal hemoglobin such as thalassemia major and minor (beta thalassemia), sickle cell disease (sickle cell syndrome, sickle cell anemia) (p. 11 paragraph 80). Said method would result in the increased proportion of fetal hemoglobin producing cells to non-fetal hemoglobin producing cells as erythropoietin acts at the cellular level by increasing gamma gene expression, thus increasing fetal hemoglobin. As set forth above, gamma globin gene expression inherently occurs in BFU-E Cells and hematopoietic/erythroid bone marrow stem cells.

Said agent of Klaus et al is administered with a second therapeutic agent such as exogenous erythropoietin or G-CSF (p.23 paragraph 187, p. 31 claim 15). The method of Klaus

Art Unit: 1645

et al is performed *in vivo* or *ex vivo* (in vitro) (abstract) and the agent is administered to primates e.g. humans or a cell (p. 1 paragraph 10).

Klaus et al teaches that the compound is an hydroxamate (iron chelator – p. 31 claim 36) or structural mimetics of 2 oxo-glutarate (paragraph 110 p. 14). Said 2 oxoglutarate mimetic will inherently inhibit (HIF) prolyl hydroxylase competitively with respect to 2 oxoglutarate and non-competitively with respect to iron.

Klaus et al does not teach said method for treating a disorder associate with abnormal hemoglobin by administering said HIF prolyl hydroxylase inhibitor and in combination with a hydroxyurea as a second therapeutic agent.

Tung et al teaches a method for increasing endogenous gamma globin and fetal hemoglobin in a patient (in vivo, humans), the method comprising administering to the subject an agent which increases expression of the gene encoding gamma globin (p.1 lines 1-15, p.2 lines 24-33, p. 3, p5 lines 16-24). Tung et al teaches that the agent is administered in combination with a second therapeutic agent such as hydroxyurea also known to treat abnormal hemoglobin disorders such as beta-hemoglobinopathies (p. 24 lines 4-27).

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to administer a second therapeutic agent such as hydroxyurea in combination with the HIF prolyl hydroxylase inhibitor used to treat abnormal hemoglobin in the method of Klaus et al because the art teaches (Tung et al) that conventional agents such as hydroxyurea can be used in combination with other agents such as those used to increase endogenous gamma globin to treat abnormal hemoglobin disorders.

Art Unit: 1645

Status of Claims

Claims 1, 9-16, 19, 21-27, 28-33, 36 and 48-49 are rejected. Claims 17,18,34,35,37,38,46 and 47 are withdrawn. No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to OLUWATOSIN OGUNBIYI whose telephone number is 571-272-9939. The examiner can normally be reached on M-F 8:30 am- 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Oluwatosin Ogunbiyi/
Examiner, Art Unit 1645

/David J Blanchard/
Primary Examiner, Art Unit 1643